Effective control of *Staphylococcus aureus* lung infection despite tertiary lymphoid structure disorganisation

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ABSTRACT

Background: Tertiary lymphoid structures (TLS) are triggered by persistent bronchopulmonary infection with *Staphylococcus aureus*, but their roles remain elusive. The present study sought to examine the effects of B- and/or T-cell depletion on *S. aureus* infection and TLS development (lymphoid neogenesis) in mice.

Methods: C57Bl/6 mice were pre-treated with 1) an anti-CD20 monoclonal antibody (mAb) (B-cell depletion) or 2) an anti-CD4 and/or an anti-CD8 mAb (T-cell depletion) or 3) a combination of anti-CD20, anti-CD4 and anti-CD8 mAbs (combined B- and T-cell depletion) or 4) isotype control mAbs. After lymphocyte depletion, mice were infected by intratracheal instillation of agarose beads containing *S. aureus* (10^6 CFU per mouse). 14 days later, bacterial load and lung inflammatory cell infiltration were assessed by cultures and immunohistochemistry, respectively.

Results: 14 days after *S. aureus*-bead instillation, lung bacterial load was comparable between control and lymphocyte-depleted mice. While TLS were observed in the lungs of infected mice pre-treated with control mAbs, these structures were disorganised or abolished in the lungs of lymphocyte-depleted mice. The absence of $CD20^+$ B-lymphocytes had no effect on $CD3^+$ T-lymphocyte infiltration, whereas $CD4^+/CD8^+$ T-cell depletion markedly reduced $CD20^+$ B-cell infiltration. Depletion of $CD4^+$ or $CD8^+$ T-cells separately had limited effect on B-cell infiltration, but led to the absence of germinal centres.

Conclusion: TLS disorganisation is not associated with loss of infection control in mice persistently infected with *S. aureus*.